

iLCT Pipeline Research Acceleration Programme: January 2025 Project Outline

Cure Parkinson's set up the **International Linked Clinical trials (iLCT)** programme in an effort to speed up the search for disease-modifying treatments for Parkinson's with the ultimate aim of making these treatments a reality for people living with Parkinson's. The iLCT is a global programme centred around an annual two-day meeting at which a committee of over 20 world-leading Parkinson's experts evaluate, rank, and prioritise drugs and compounds – many from other disease areas – with the potential to be repurposed or repositioned to modify the progression of Parkinson's.

Where the committee feels an agent has potential, but requires more research before moving into clinical testing, they put that molecule into the iLCT Pipeline Research Acceleration Programme. For more information about this funding programme: <https://cureparkinsons.org.uk/for-researchers/apply-for-funding/ilct-pipeline-research-acceleration-programme/>

The iLCT Pipeline Research Acceleration Programme is opening for 2025 with the following timeline:

Expression of interest deadline: 28th February 2025

Full application deadline: 28th March 2025

Anticipated decision: End July 2025

Cure Parkinson's and the iLCT committee are keen to gather more information about 4 drugs. For all compounds we would be interested to see assessments of:

- Alpha synuclein
- Dopamine neuronal survival
- Locomotor behavioural evaluation (where possible)
- Evaluation of any potential sex differences
- Brain penetrance (where possible)

1. Empagliflozin

- This is a competitive inhibitor of sodium-glucose co-transporter 2 (SGLT2) with antihyperglycemic activity. Epidemiological evidence suggests that administration of this drug is associated with reduced risk of Parkinson's.
- We are seeking data surrounding target engagement, as well as additional *in vivo* work determining neuroprotective potential.
- Model systems to be used:
 - Patient-derived neuronal cell models of Parkinson's
 - Non-toxin *in vivo* Parkinson's models (transgenic or alpha synuclein)
- Optional assessments:
 - Mitochondrial function, particularly receptor-mediated mitophagy
 - USP30 inhibition

2. Theracurmin

- Despite preclinical results indicating interesting biological properties, curcumin has poor bioavailability. Theracurmin is a slow-release nanoparticle formulation of curcumin that enhances the pharmacokinetics of the active agent.
- We are particularly interested in assessing dosing ranges and brain penetrance in *in vivo* models of Parkinson's.
- Model systems to be used:
 - Any validated rodent alpha synuclein model(s) of Parkinson's
- Additional required assessments:
 - Dosing ranges
- Optional assessments:
 - Anti-oxidant effects
 - Anti-inflammatory effects

3. Pyridoxal-5'-phosphate

- This is the biologically active form of vitamin B6. It is a cofactor for more than 70 human enzyme-catalysed reactions, and has been reported to be neuroprotective.
- Cure Parkinson's would like to gather more pre-clinical data on this compound. Specifically, we would like to see an evaluation of neuroprotective potential.
- Model systems to be used:
 - Patient-derived neuronal cell models of Parkinson's
 - *In vivo* models of Parkinson's, preferably any validated alpha synuclein model(s)
- Optional assessments:
 - Mitochondrial function
 - Anti-inflammatory effects
 - Target engagement

4. Alogliptin

- This is a dipeptidyl peptidase-4 (DDP-4) inhibitor that is used in the treatment of diabetes. Epidemiological investigations have indicated that treatment with this agent is associated with a reduced risk of Parkinson's.
- We are interested in assessing alogliptin in pre-clinical models of Parkinson's.
- Model systems to be used:
 - Non-toxin *in vivo* model of Parkinson's, preferably any validated alpha synuclein model(s)
 - Patient-derived neuronal cell models of Parkinson's
- Optional assessments:
 - Target engagement
 - Anti-inflammatory effects

Please note, that although we have outlined model systems to be used, other model systems may be considered providing a valid rationale is given

Drug CV forms and iLCT dossiers (containing detailed information on the scientific background, summary of the intervention, assessment of target engagement, preclinical data, and clinical history including dosing, safety/tolerability, pharmacokinetics/pharmacodynamics and brain penetrance) have been prepared for each of these therapies. These are available upon request from Research@cureparkinsons.org.uk.

Applications testing more than one of the candidate agents may be viewed more favourably, but a minimum of one of these therapies must be included in each application.

Max project cost:

- Up to £250,000 GBP, preferably less.
 - Applications must provide a detailed and realistic justification of project costs
 - Applications for the maximum £250,000 grant should include some of the optional additional assessments

Max project duration:

- Up to 18 months, preferably shorter. (Projects should begin by the end of 2025.)
 - Applications must provide a detailed and realistic justification of the project timeline
 - Applications for the maximum 18-month period should include some of the optional additional assessments

Please fill in the expression of interests form in order to be considered for a full application

To be considered for funding, please fill in the expression of interest form and email to research@cureparkinsons.org.uk **by 5pm (GMT) Friday 28th February 2025.**

Anonymous expressions of interest will be reviewed internally by the Cure Parkinson's research team on a rolling basis and will be used to invite full applications for those projects most closely aligned with the goal of the funding call.

Invitations to submit a full application will be sent out no later than three weeks prior to the full application deadline.

Only full applications that have been invited for submission will be sent for external peer review and further considered for funding by our independent research committee.

For more information about the application process, please visit

<https://cureparkinsons.org.uk/for-researchers/apply-for-funding/ilct-pipeline-research-acceleration-programme/>.

To submit a full application, please email Research@cureparkinsons.org.uk with your completed application and budget forms alongside a signed and dated letter from the host institution confirming support for the application based on the terms and conditions outlined in the Cure Parkinson's Grant Contract.

The deadline for full applications is **5pm (GMT) Friday 28th March 2025.**